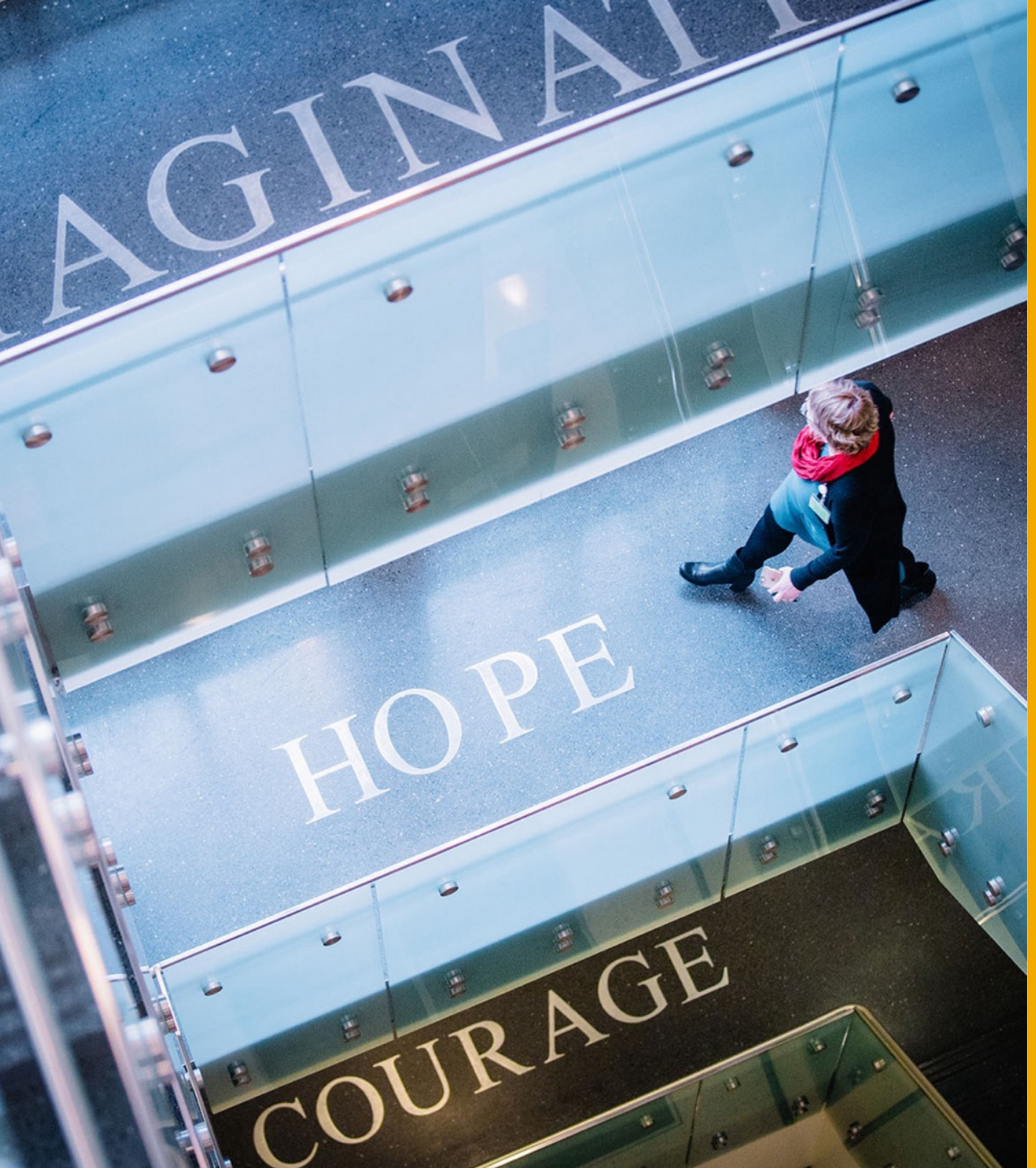


Where Science Becomes Hope

USING PATHOLOGIC RESPONSE TO DETERMINE DE-ESCALATION OF SURGERY AND NEED FOR ADJUVANT THERAPY--CON

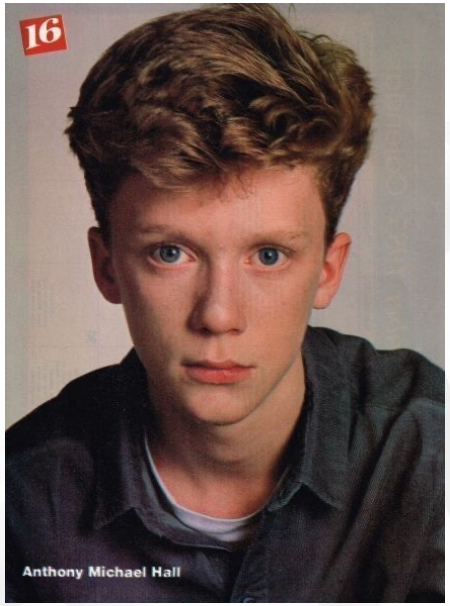
Keith A. Delman, MD

EMORY WINSHIP CANCER INSTITUTE
National Cancer Institute-Designated Comprehensive Cancer Center

NCI Designated Comprehensive Cancer Center

DISCLOSURES

No financial disclosures



It’s a bit unfair to have to debate either the country’s favorite doctor prodigy or a generationally famous child-actor.

WHY DE-ESCALATION BASED ON PATHOLOGY IS A BAD IDEA

- We don’t have data on de-escalation of surgery
- We do have data on outcomes with neo-adjuvant therapy and pathologic response
- True follow up time matters, not actuarial studies have continuously proven that time changes outcome
- Pathology is good, but not great and it has always relied on the tissue being removed

WHY DOES TIME MATTER???

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

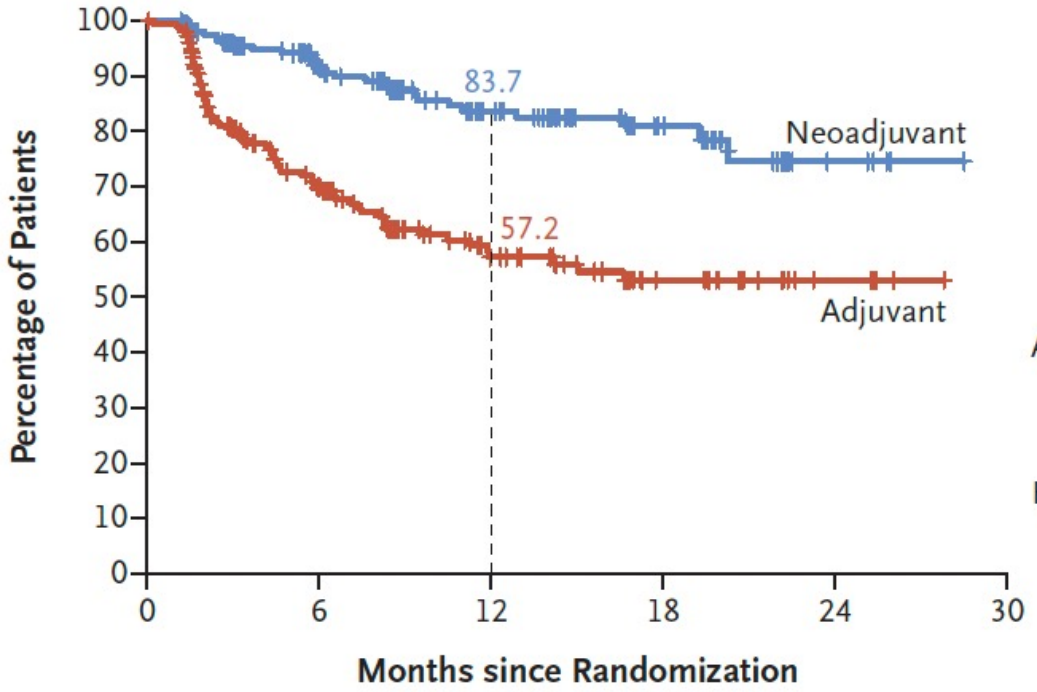
Hormone Therapy and the Progression of Coronary-Artery Atherosclerosis in Postmenopausal Women

Late radiation morbidity following randomization to preoperative versus postoperative radiotherapy in extremity soft tissue sarcoma

Aileen M. Davis[a,j,*], Brian O'Sullivan[b,j], Robert Turcotte[c], Robert Bell[b,d,j], Charles Catton[b,j], Pierre Chabot[e], Jay Wunder[b,d,j], Alex Hammond[f], Veronique Benk[g], Rita Kandel[d,j], Karen Goddard[h], Carolyn Freeman[c], Anna Sadura[i], Benny Zee[i], Andrew Day[i], Dongsheng Tu[i], Joseph Pater[i], A Canadian Sarcoma Group and NCI Canada Clinical Trials Group Randomized Trial

[a]*Toronto Rehabilitation Institute, Canada,* [b]*Princess Margaret Hospital, Toronto, Canada,* [c]*McGill University Health Center, Montreal, Canada,* [d]*Mount Sinai Hospital, Toronto, Canada,* [e]*Hopital Maisonneuve-Rosemont, Montreal, Canada,* [f]*London Regional Cancer Centre, Ont., Canada,* [g]*Toronto-Sunnybrook Regional Cancer Centre, Ont., Canada,* [h]*BC Cancer Agency, Vancouver, Canada,* [i]*NCI Canada Clinical Trials Group, Cancer Research Institute, Ont., Canada,* [j]*University of Toronto, Canada*

NADINA TRIAL



No. of Events/ Total No. of Patients	
Neoadjuvant	28/212
Adjuvant	72/211

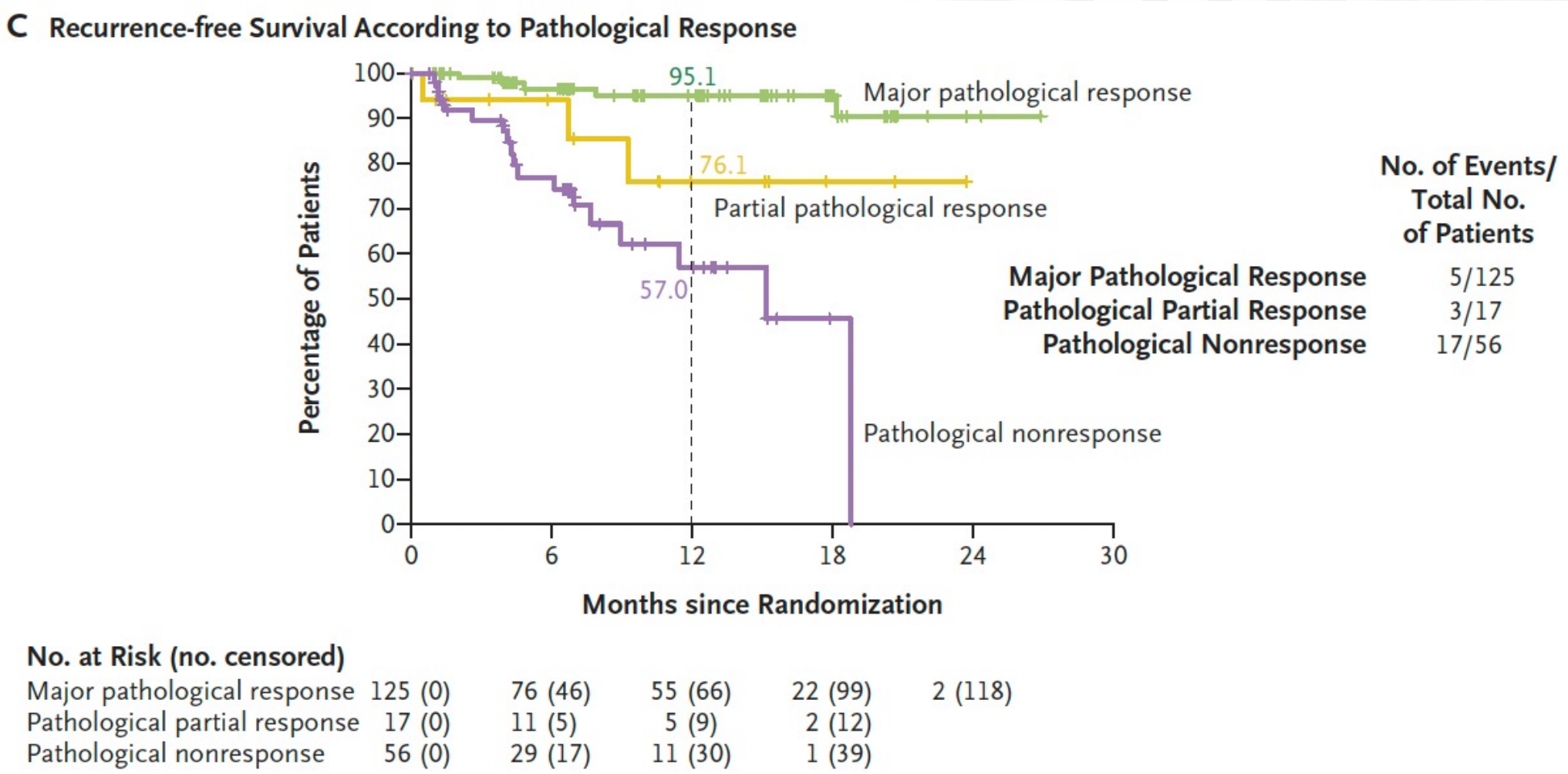
Adjusted difference in restricted mean survival time, 8.00 mo (99.9% CI, 4.94–11.05); P<0.001

Hazard ratio for progression, recurrence, or death, 0.32 (99.9% CI, 0.15–0.66)

No. at Risk (no. censored)					
Neoadjuvant	212 (0)	126 (71)	77 (111)	34 (152)	5 (179)
Adjuvant	211 (0)	100 (57)	53 (89)	23 (116)	6 (133)

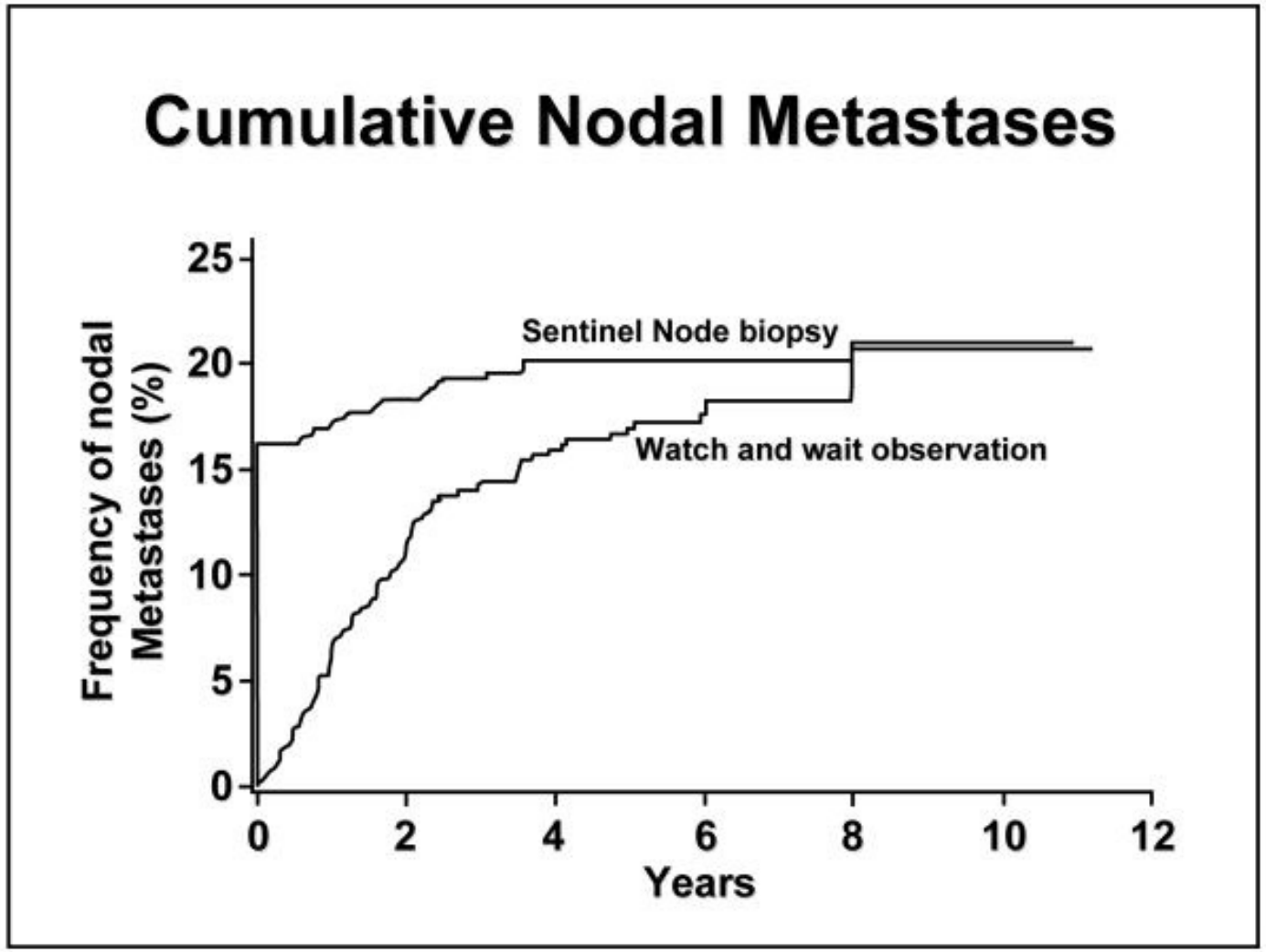
Blank C, et al. N Engl J Med 2024 Jun 2.epub ahead of print.

NADINA TRIAL II



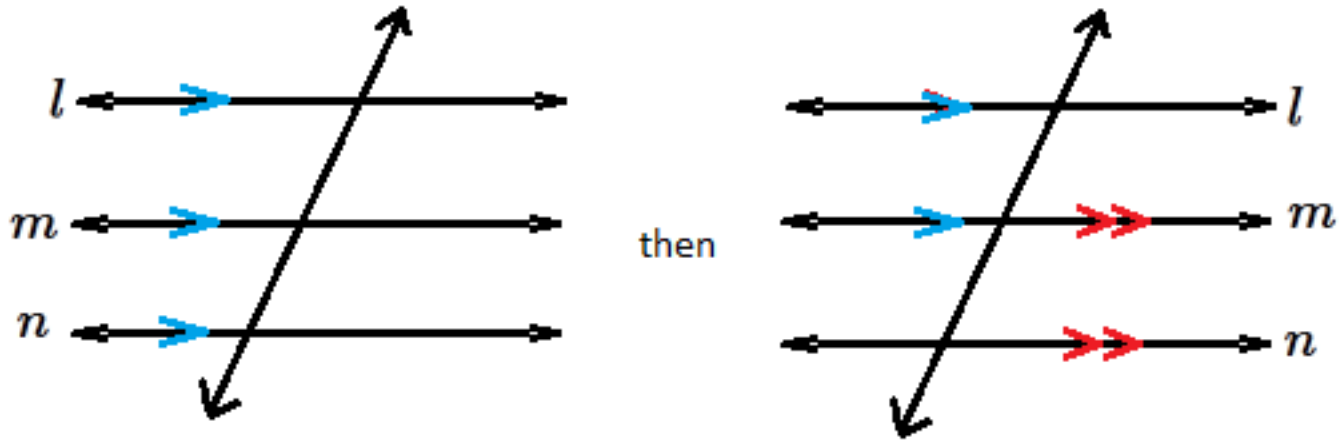
Blank C, et al. N Engl J Med 2024 Jun 2.epub ahead of print.

MSLT-1 NODAL EVENTS



Slide courtesy of Mark Faries

TRANSITIVE PROPERTY



If $l \parallel m$ and $m \parallel n$ then $l \parallel n$.

TRANSITIVE PROPERTY: MSLT-1 AND MSLT-2/DECOG

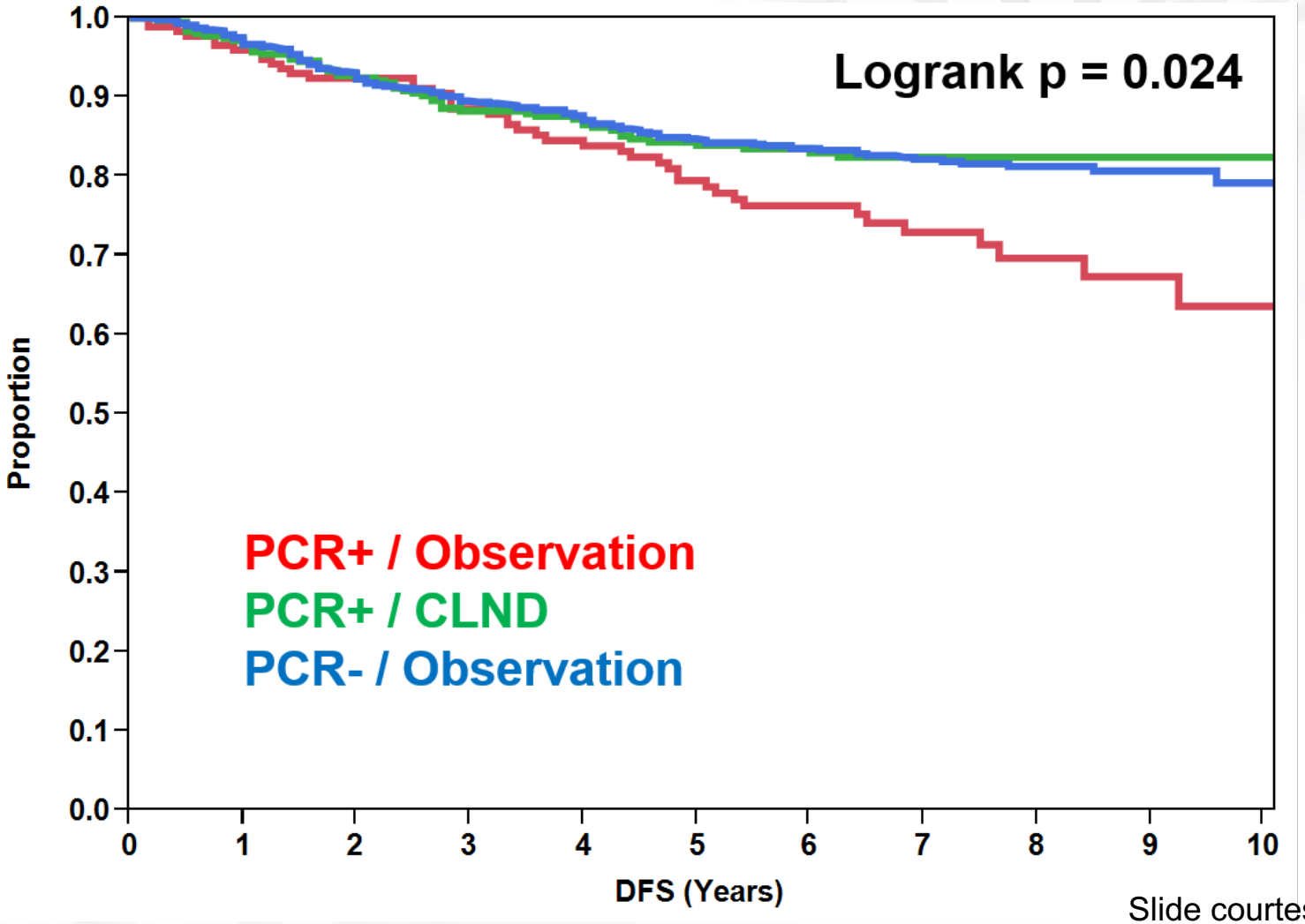
- IF MSLT-1 OS in node + patients:
  - SLN + patients with early dissection: 70% 5 yr OS
  - OBS → completion dissection: 50% 5 yr OS

- And IF MSLT-2/DeCOG:
  - No impact from completion lymph node dissection

- Then: Removal of disease early matters

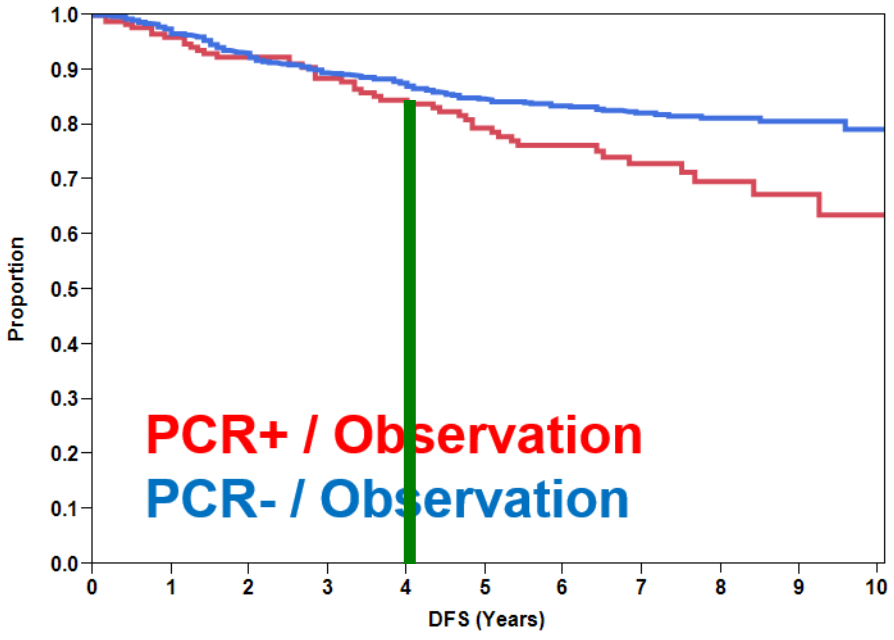
Morton DL, et al. **N Engl J Med**. 2014 Feb 13;370(7):599-609
Faries M, et al. **N Engl J Med**. 2017 Jun 8;376(23):2211-2222
Leiter U, et al. **Lancet Oncol**. 2016;17(6):757–767.

DISEASE-FREE SURVIVAL



Slide courtesy of Kelly McMaster

IMPACT OF PCR STATUS AND CLND ON DFS



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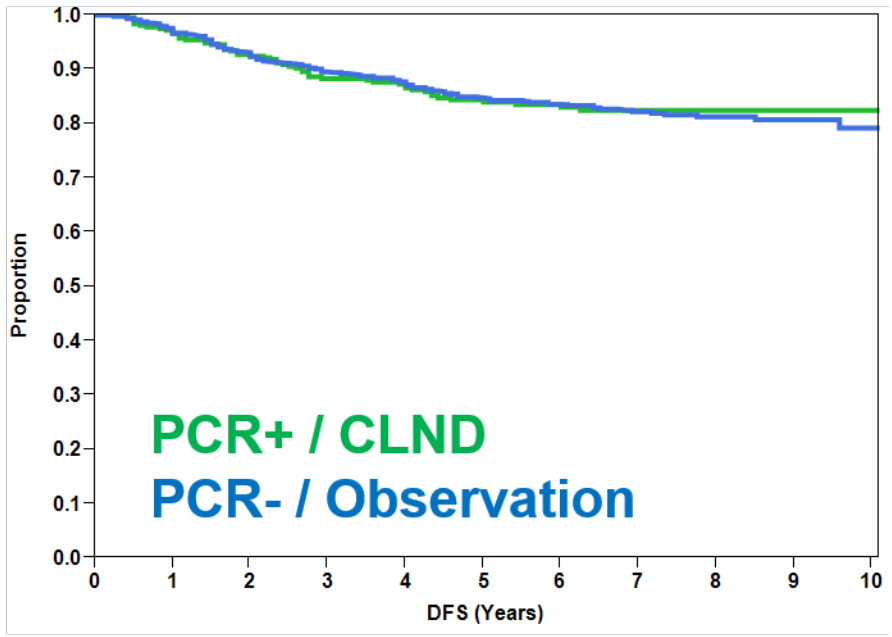
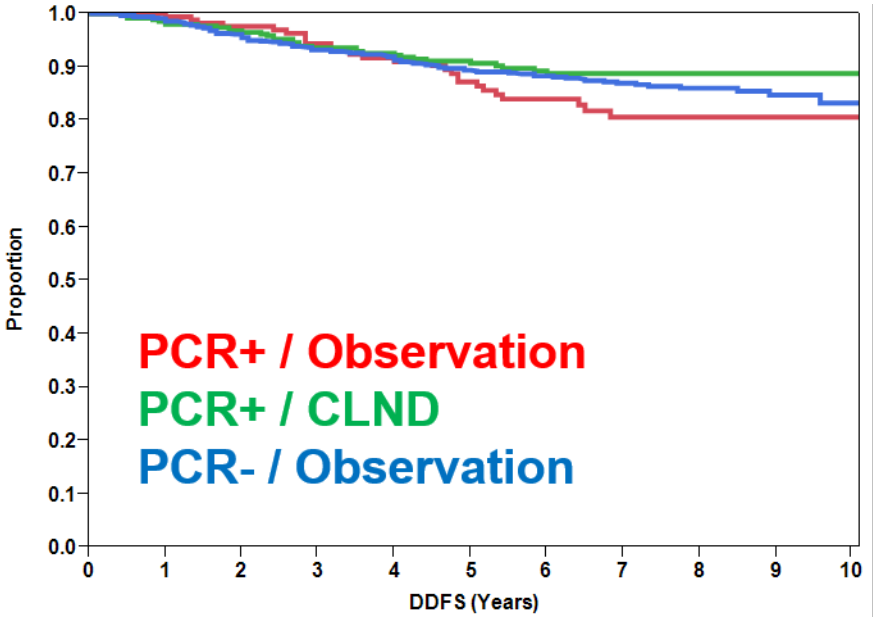


Logrank

Slide courtesy of Kelly McMaster

PATTERNS OF RECURRENCE

Distant Metastasis



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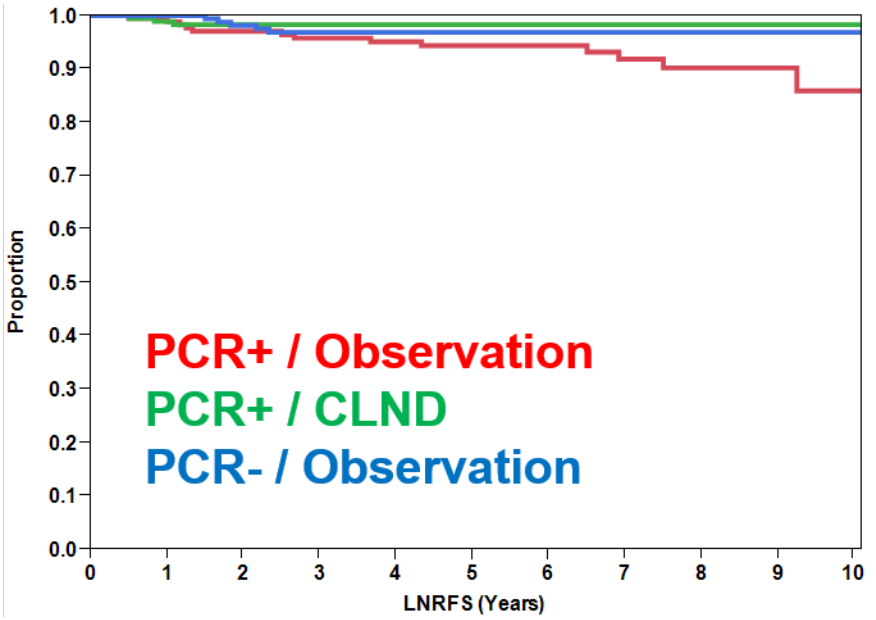
Lymph Node Recurrence



Logrank p = 0.0261

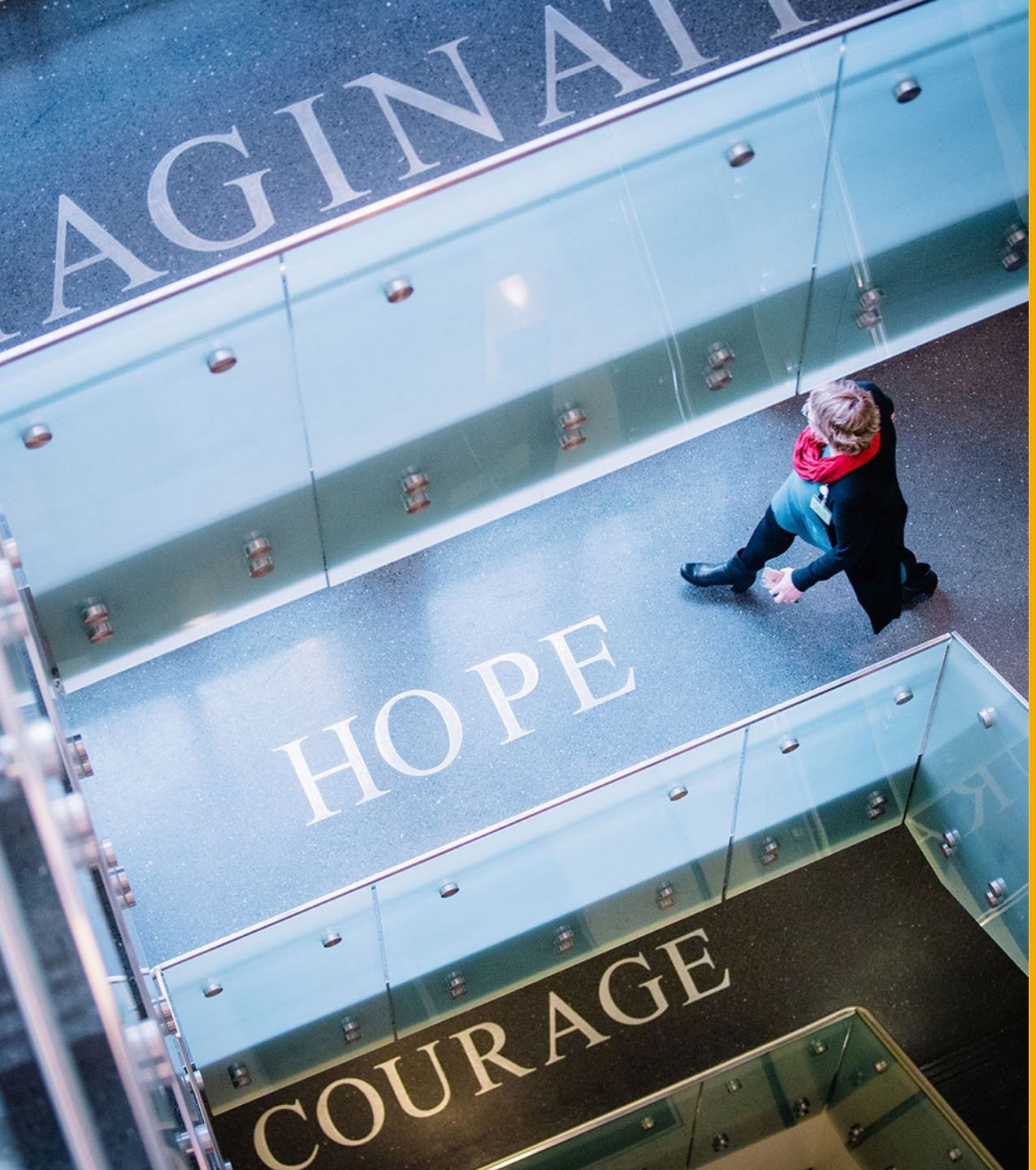
Slide courtesy of Kelly McMaster

RECURRENCE IN A NODAL BASIN MATTERS

- Early removal of disease has an impact
- Histologic assessment may not accurately reflect the entire status of the nodal basin (PCR in Sunbelt) need more resources to assess the entirety of the specimen
- Delayed recurrences may impact survival
  - Not enough follow up time
- Surgery is safe and effective with a complication profile far lower than systemic therapy

LET'S NOT THROW THE BABY OUT WITH THE BATHWATER

- We have effective therapy that works for documented disease (original trials)
- Surgery is safe and effective
- We do not have long term follow up yet



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